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Fr m: Qazi, Sabiha
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Please provide following references.

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DHEA

Thank you.

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DHEA: "Miracle" drug?

SAUL KENT

A natural hormone with an elusive biologic role may have useful anticancer properties as well as aiding in weight reduction

In recent months a great deal of controversy has been raised about a new "miracle" weight reducer—the starch blocker—which represents an approach to the weight-conscious who do not want to deprive themselves of fattening foods. It may turn out, however, that a natural hormone will provide just such a means of weight reduction, enabling us to eat as much as we want and still stay thin. This intriguing possibility came to light during animal cancer studies with dehydroepiandrosterone (DHEA) and has yet to be substantiated in humans.

Anticancer effect

In fact, DHEA is a common steroid compound produced in very large quantities by our adrenal glands. There is far more DHEA circulating within our bodies than any other steroid—about 20 times more. Yet, until recently, the biologic functions of DHEA were a complete mystery. Although it appeared to be a hormone, it exhibited none of the qualities normally associated with hormonal activity.

Dr. Arthur Schwartz at the Fels Research Institute at Temple University first became interested in DHEA as a result of a report from British endocrinologist R.D. Bulbrook, who found that women with breast cancer have lower-than-normal urine levels of androsterone and etiocholanolone, both of which are derived primarily from DHEA.[1] Since urine levels of these two steroids reflect plasma concentrations of DHEA, this suggested that blood levels of DHEA may be reduced in women with breast cancer.

Saul Kent is a science writer and life extension speaker.

Bulbrook then conducted a prospective study in which he measured urine levels of androsterone and etiocholanolone over a 10-year period in 5,000 apparently healthy women. In 1971, he reported that 27 of these women had developed breast cancer and that these were women who had lower-than-normal levels of DHEA derivatives years before there was evidence of breast cancer—as long as 9 years prior to diagnosis.[2] This provided further evidence that low levels of DHEA may be associated with breast cancer.

In a preliminary tissue culture study, Schwartz added DHEA to a culture medium containing two potent chemical carcinogens—dimethylbenz(a)anthracene (DMBA) and aflatoxin B_1. He discovered that DHEA was remarkably successful in protecting cultured rodent cells against DMBA and aflatoxin B_1, whereas other related steroids were not effective.

He then gave DHEA (450 mg per kilogram of body weight 3 times per week) to C3H mice, which are genetically bred to develop breast tumors, but no tumors had yet appeared in the DHEA-treated animals.[3] Since C3H mice all carry the mammary tumor virus, the DHEA animals eventually did develop cancer, but the onset of these tumors was delayed markedly.

Schwartz believes that DHEA's anticancer effect may be the result of its ability to inhibit the activity of the enzyme glucose-6-phosphate dehydrogenase (G-6-PDH). This enzyme generates a compound called nicotinamide-adenine dinucleotide phosphate (NADPH), which is involved in the activation of chemical carcinogens within the body. It is possible that DHEA protects against cancer by limiting the

production of NADPH.

DHEA has also been found to block cell division by inhibiting DNA synthesis, which depends upon the action of NADPH.[4] This provides further evidence that DHEA's inhibition of G-6-PDH may be the mechanism by which it interferes with carcinogenesis.

Anti-obesity effect

When Schwartz was analyzing the anticancer effect of DHEA, he discovered that the experimental animals had gained significantly less weight as they grew older than did the control animals. He found that the weights of the DHEA-treated mice were comparable to those found in chronically underfed animals, even though the DHEA animals ate as much as or more than the control animals.[3]

Apparently, DHEA was keeping body weight down without suppressing appetite or restricting food intake. Dr. Schwartz speculates that DHEA may produce this effect by blocking G-6-PDH, which is involved in lipogenesis (fat formation). The DHEA animals had less body fat and were more active than the control animals.

Since this initial experiment with cancer-prone mice, Schwartz has been able to duplicate the anti-obesity effect of DHEA in other strains of mice as well as in rats. In one study, he found that DHEA could even prevent weight increase in mice genetically bred to become obese in adulthood.[5]

Many scientists have found that laboratory mice and rats maintained on a calorically restricted diet have a significantly lower tumor incidence than normally fed animals.[6] Thus, DHEA's ability to inhibit tumor formation in mice may be the result of its ability to maintain a lower body weight.

In work with aged Sprague-Dawley rats,[5] Schwartz found that the average weight in animals treated with DHEA was reduced from 650 to 550 g although they continued to eat as much or more

than they did before the experiment started. Of further interest was the fact that the DHEA animals ate less than the controls when they were given a high-fat diet (11% fat), but ate more than controls when the fat content of their diet was lowered to 5%. This finding suggests that DHEA may suppress the desire for fatty food.

Anti-aging effect

Another effect of caloric restriction in animals is a significant extension of mean and maximum life spans. DHEA-treated mice had a considerably younger appearance than control animals, and at 14 months of age, they showed "less coarsening and graying [of the hair] and appeared younger looking than the controls."[3]

This suggests that DHEA may have an anti-aging effect as well as anticancer and anti-obesity effects. Thus far, Schwartz has not conducted any life-span studies with DHEA-treated animals, but he did study the effects of DHEA in 25 aged (2-year-old) Sprague-Dawley rats[5] and found that mortality was slightly but not significantly lower in the DHEA-treated rats than in the controls.

Also relevant is the report that DHEA apparently is greatly reduced in the bloodstream of humans with advancing age. DHEA levels peak at about age 25 and drop off rapidly thereafter, diminishing by up to 95% by the age of 85 or 90.[7] This may be further evidence that DHEA is related to the aging process, and suggests that by keeping our blood levels of DHEA at peak values, we might be able to remain youthful for extended periods of time.

Prospects

One problem in extrapolating to humans from the animal experiments performed thus far is that DHEA has only been effective in large doses, apparently because much of the compound is degraded in the liver before it reaches the bloodstream. To overcome this problem, scientists at Temple University have been synthesizing chemically active analogs of DHEA to lower the dose requirements for the drug. They have found that one of these analogs—DHEA-sulfatide—is a more potent inhibitor of G-6-PDH than DHEA, so that it may be more effective than DHEA in lowering body weight or as an anticancer or anti-aging drug.

Unpublished work by Schwartz and his associates indicates that DHEA and its analogs can prevent both lung cancer and colon cancer in laboratory animals. Doctors at M.D. Anderson Hospital in Houston are interested in determining whether DHEA can prevent or reverse cancer in humans, and they want to give it to women at risk of breast cancer or in the early stages of the disease. Other physicians at Memorial Sloan-Kettering Cancer Center in New York are planning a similar trial in patients at risk of colon cancer. Such clinical trials may in addition be useful in evaluating DHEA's potential as a weight-reducing agent in humans.

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